REMARKS

Claims 1-13 and 15-71 are pending. All claims are rejected.

Obviousness –Type Double Patenting Rejections are Traversed

Shytle, in view of Cliffe

The Examiner stated that claims 1-14 and 16-71 are rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 7-11 of U.S. Patent No. 6,734,215 to Shytle, *et al.* (Shytle) , in view of U.S. Patent No. 5,204,470 to Cliffe (Cliffe). It has been assumed that the Examiner intended to indicate "claims 1-13 and 15-71," claim 14 having been canceled.

In view of the Terminal Disclaimer regarding Shytle, submitted herewith, any asserted basis for the foregoing rejection is now moot. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. §112, Second Paragraph, are Traversed

Claims 2, 7, 10, 52, 70, and 71 are rejected as allegedly indefinite under 35 U.S.C. §112, second paragraph, based on their recitation of the term "mecamylamine analog." Office Action at page 3. In view of the following remarks, Applicants respectfully traverse the rejection.

At page 10 of Applicants' specification, analogs of mecamylamine are discussed:

> In addition, the various stereoisomers and substituted analogs of mecamylamine have been tested for activity (Stone et al., J Med Chem 5(4): 665-90, 1962, hereby incorporated by reference). Activity, as tested in rats by nicotine convulsions and pupil dilatation, was routinely lost with larger substitutions for the methyl groups. Both methyl or dimethyl groups on the amino group were more active than other substituents.

It is Applicants' position that one of skill in the art, in view of at least the disclosure quoted above, would readily understand the meaning of the term "analog" as presently recited in Applicants' claims.

In Applicants' specification, the discussion of active variations represented by the methyl and dimethyl substitutions on the amino group provides guidance as to the character of mecamylamine analogs encompassed by Applicants' claims. Stone, *et al.*,

incorporated by reference, provides further guidance. Stone, *et al.* provides confirmation of the structure of mecamylamine and a systematic exploration of activity of a number of mecamylamine analogs. One of skill in the art, considering the guidance provided by Stone, *et al.* and using knowledge in the art, would readily understand what is intended by Applicants' recitation of mecamylamine "analog."

Accordingly, the use of the term "analog" in Applicants' claims would not be considered indefinite by one of ordinary skill in the art in view of knowledge in the art and the disclosure of Applicants' specification.

Because all asserted bases for rejection of Applicants' claims as indefinite have been properly traversed, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. §103(a) are Traversed

Crooks, in view of Suzuki

Claims 1-13 and 15-71 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over U.S. Patent No. 5,691,365 to Crooks, *et al.* (Crooks), in view of Suzuki, *et al.* (Suzuki). The Examiner stated that:

> Crooks et al. teach nicotine analogs that have nicotinic receptor antagonist properties are useful in treatment of cognitive disorders such as Alzheimer's disease and for the treatment of Parkinson's disease. (abstract). . . .
>
> Crooks et al. do not teach the specific nicotine receptor antagonist such as mecamylamine for treating cognitive deficits in learning and memory, bronchial inhalation, additionally employing atypical neuroleptic drug.
>
> Suzuki et al. report that mecamylamine is a nicotinic receptor antagonist. (abstract).

Office Action at pages 4-5. In view of the following remarks, Applicants respectfully traverse the rejection.

All of Applicants' pending claims recite either "a partial nicotine agonist" or "mecamylamine, a mecamylamine analog, or a mecamylamine stereoisomer." No nicotine antagonists are presently claimed. As noted in Applicants' specification at page 8, referring to the beneficial effects of the invention as presently claimed: "We believe that these effects of mecamylamine are due to a previously unrecognized partial agonist activity of mecamylamine at

low doses." Accordingly, the presently claimed aspect of the disclosed invention relates to "partial nicotine agonists" and to mecamylamine in particular.

The Examiner acknowledged that Crooks did not specifically teach mecamylamine, but cited Suzuki as having taught that mecamylamine was a nicotine receptor antagonist. Further, Applicants note that Crooks discussed the compounds disclosed therein as a "new class" of nicotine antagonists. See Crooks at col. 6, line 26; and at col. 13., line 56. Also, Crooks stated that "[t]he inventors show the molecules described are binding to the antagonist site in their unprotonated forms and that the binding mode involves interaction of the quaternary ammonium nitrogen with the anionic site of the receptor." Crooks at col. 12, lines 55-58. Comparisons of the disclosed compounds with inhibition produced by "the classical nicotine inhibitors" mecamylamine and DHBE were provided. See Crooks at col. 16, lines 62-64. Thus, Crooks taught a very particular class or group of compounds for the methods discussed therein, not nicotine antagonists generally. However, it should be noted that, assuming for the sake of argument only that *any* general antagonist activity is taught by Crooks, no partial agonism is taught or suggested.

Further, the lack of consideration of mecamylamine by Crooks despite the inclusion of that compound as a comparative example would have provided no motivation for one of skill in the art to examine mecamylamine as a possible compound for treatment of any of the disorders disclosed by Crooks. In fact, the use of mecamylamine as a comparative example without any consideration by Crooks of that compound for use in the methods discussed would have discouraged the skilled artisan from any use of mecamylamine in such methods. In this regard, the disclosure of Crooks actually *taught away* from the presently claimed invention. Suzuki added nothing to counter this teaching away, in that Suzuki only disclosed the classic antagonist activity of mecamylamine in the nicotine withdrawal experiments discussed therein.

For at least the reason that no combination of Crooks and Suzuki taught or suggested any methods for treatment of the presently recited disorders using partial nicotine agonists, or mecamylamine in particular, none of Applicants' claims would be considered obvious by one of ordinary skill in the art in view of those references. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Conclusion

All alleged bases for rejection of Applicants' pending claims have been properly traversed or rendered moot. Accordingly, the present application is in condition for immediate allowance, and early notice to that effect is earnestly solicited.

The Examiner is invited to contact Applicants' undersigned representative using the information provided below if she has any questions or comments regarding this Reply.

Respectfully submitted,

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